Armed Forces College of Medicine

THYROID GLAND

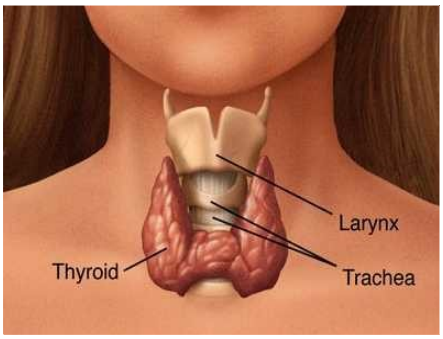
INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture the student will be able to:

1. List the hormones secreted from the thyroid gland
2. List the steps of thyroid hormones synthesis.
3. Outline the mechanism of storage and excretion of thyroid hormones.
4. Illustrate the role of hypothalamus and pituitary gland in regulating thyroid function
5. Describe the pituitary-thyroid axis
6. Summarize the effects of thyroid hormones in homeostasis and development

Endocrine module 3

Hormones of thyroid gland



- ***Thyroid hormones*: *thyroxin*: *T4* and *tri-iodothyronine*: *T3***, by the thyroid follicle cells: it affects the iodine & the general body metabolism.
- ***Thyrocalcitonin: TCT:*** *from the parafollicular cells. TCT together* with PTH and 1,25 dihydroxycholecalciferol (extrathyroidal hormones) maintain a normal plasma Ca^{2+} and affects the body Ca metabolism.

Thyroid follicles

Importance of iodine for thyroid hormone production

- Thyroid hormones are unique biological molecules in that they incorporate iodine in their structure.
- Thus, adequate iodine intake **(diet, water)** is required for normal thyroid hormone production.

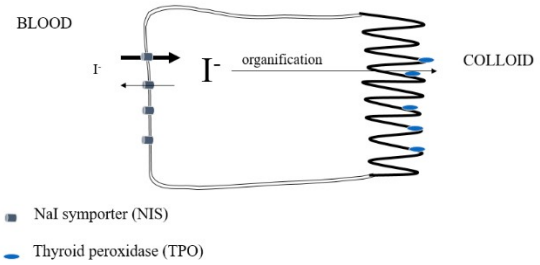
- **Major sources of iodine:**

- iodized salt - iodated bread - dairy products - shellfish

- **Minimum requirement:**

75 micrograms/day

- **Ion transport by the thyroid follicular cell**



- **Production of Thyroglobulin**

Pituitary produces TSH which binds to a **plasma membrane-bound, G protein-coupled receptor** on thyroid follicle cells.

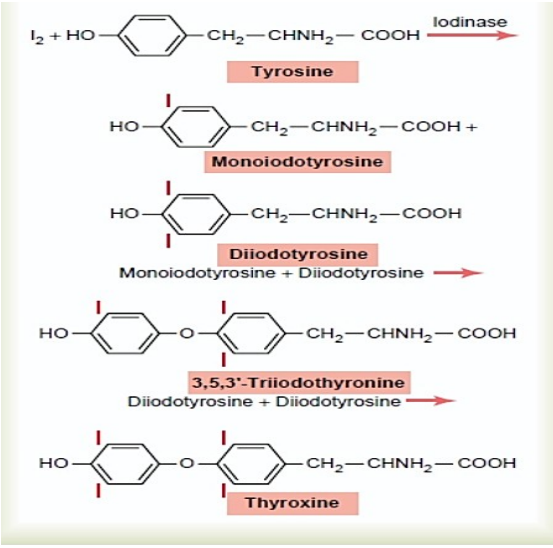
Specifically, it activates a Gs-coupled receptor, resulting in **increased cAMP production and PKA activation**.

The follicle cells of the thyroid produce thyroglobulin.

Thyroglobulin is a very large **glycoprotein**. It is the precursor of T4 and T3

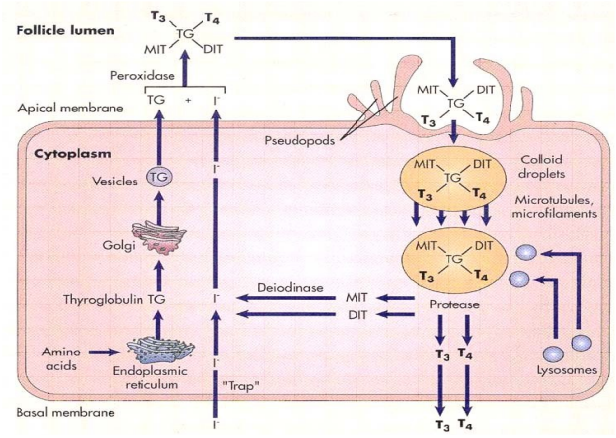
Thyroglobulin is released into the colloid space, where its tyrosine residues are iodinated.

This results in tyrosine residues which have one or two iodines attached (mono-iodo tyrosine or di-iodo tyrosine).



- **Steps of Thyroid hormones synthesis**

1. **Uptake of iodide and its activation to iodine.**
2. **Iodination of tyrosine residues to MIT and DIT.**



- **T3 and T4**
- ***Rate of T_4 & T_3 secretion:***

the thyroid gland secretes about 70 μg /day.

T_4: thyroxine (93%). T_3: (7%).

- ***Level of thyroid hormones in blood.***

Total T_4 : about 8-12 μg/dl Total T_3: about 0.15 μg/dl

Bound T_4 : about 99.98 % Bound T_3 : about 99.8 %

Free T4 : about 2 ng/dl Free T3 : about 0.3 ng/dl

- ***Carriage of thyroid hormones:***

*A*lbumin, thyroxine binding prealbumin (TBPA),

thyroxine binding globulin (TBG)

- ***Characters of plasma protein binding to thyroid hormones.***

More than 99% of thyroid hormones is bound.

Less than 1% is free.

Affinity of globulins is higher than albumin or prealbumin to thyroid hormones.

- **Mechanism of action of thyroid hormones**

Thyroid hormones bind to thyroid receptors (mainly in the nucleus).

*T3 is more active than T4 because it is:

1. More free (less bound to plasma proteins).

2. More affine to the thyroid receptors (10-15 fold greater affinity than T4).

rT3 is non active because it does not bind to the thyroid receptors.

- **Important features of thyroid hormone function in the nucleus**

1. They activate the genetic mechanisms for the formation of many types of intracellular proteins-probably 100 or more. Many of these are enzymes that promote enhanced intracellular metabolic activity in all cells of the body.
2. Once bound to the intranuclear receptors, the thyroid hormones can continue to express their control functions for days or even weeks.

Effects of thyroid hormones

I- Effects on metabolism:

1.On cell metabolic activity: calorigenesis & increase O2consumption by:

a- Effects on mitochondria: they increase in size & number (in most cells), which leads to an increase in the rate of ATP formation.

Excessive increase in thyroid hormones produces mitochondrial swelling and increased uncoupling of oxidative phosphorylation.

Increased uncoupling results in a smaller increase ATP & a greater loss of heat.

b- Effects on cell membrane ions transport: there is increased

activity of Na/K ATPase enzyme, which leads to increased transport of Na& K through the cell membrane of all body cells and increased energy consumption.

2- Effects on carbohydrate metabolism: stimulate all aspects of carbohydrate metabolism. They increase insulin secretion, glucose absorption by the GIT, glucose uptake by the cell, glycolysis & gluconeogenesis.

3- Effects on fat metabolism:

a- all aspects of fat metabolism are stimulated and cause mobilization of lipid from fatty tissues (lipolysis), increased free fatty acid oxidation and depletion of fat stores.

b- Effects on plasma lipids: thyroid hormone, *decrease plasma cholesterol due to:

- increased secretion of cholesterol in bile and stools.
- increased number of LDL receptors on liver cells which leads to rapid removal of LDL from plasma.
- increased oxidation of cholesterol by cells.

4- Effects on protein metabolism: anabolic hormone, it increases protein synthesis all over the body.

5- Effects on vitamin metabolism: the general increase in enzymes activity leads to a general increase in the body needs for vitamins: the coenzymes.

6- Effect on basal metabolic rate (BMR: BEE: basal energy expenditure) and body weight: the normal amount of thyroid hormones is responsible for a normal BEE of about 40Calories / hr / m2 surface area in a normal adult male & a normal body weight due to a normal appetite with a normal food intake & normal energy consumption (energy balance).

II- Effects on body systems:

a- Primary effect: the majority of the body systems are stimulated by a direct hormonal action.

b- Secondary effect: the various body systems are stimulated by the increased metabolism: calorigenic action. This action causes an increase in O2 consumption in most tissues e.g. CVS , respiratory , GIT ,muscular , and endocrine systems.

*In some tissues O2 consumption is not increased e.g. adult brain, lymph nodes, spleen, testes & uterus .

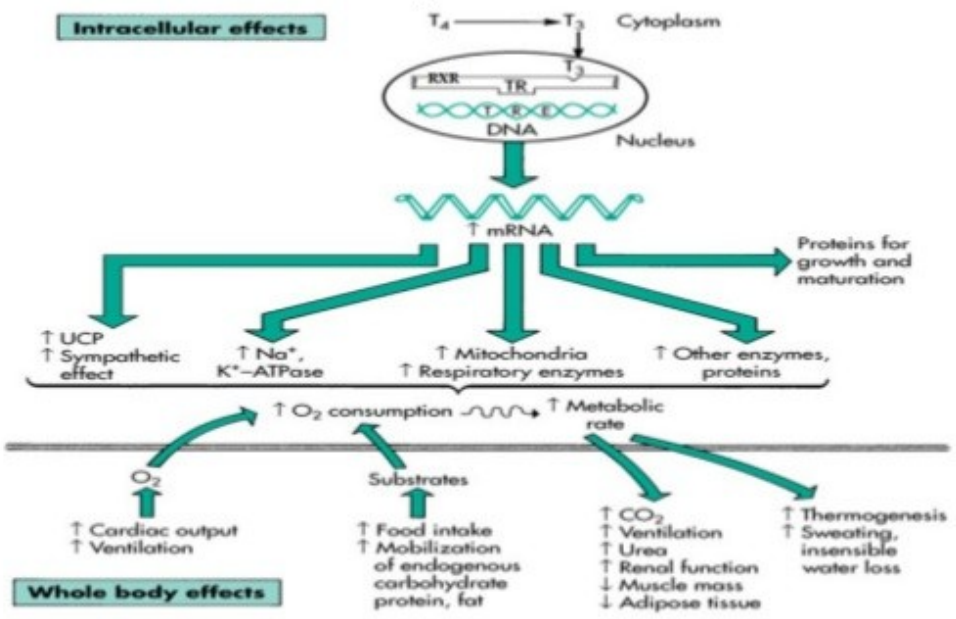
*In the anterior pituitary O2 consumption is decreased.

III- Effects on growth:

a – Mental growth & development of brain: it is important during fetal & first few years of postnatal life for normal mental development, especially of the nervous system. It induces neuronal, axonal & nerves ending formation.

b - Skeletal growth: bones & epiphyses grow. Bones are affected more than soft tissues.

c –Sexual growth: together with sex hormones responsible for sexual growth.



In SUMMARY: the thyroid hormones are essential for:

- **Normal development: physical, mental & sexual in young.**
- **Normal functions: physical, mental and sexual in adults**.

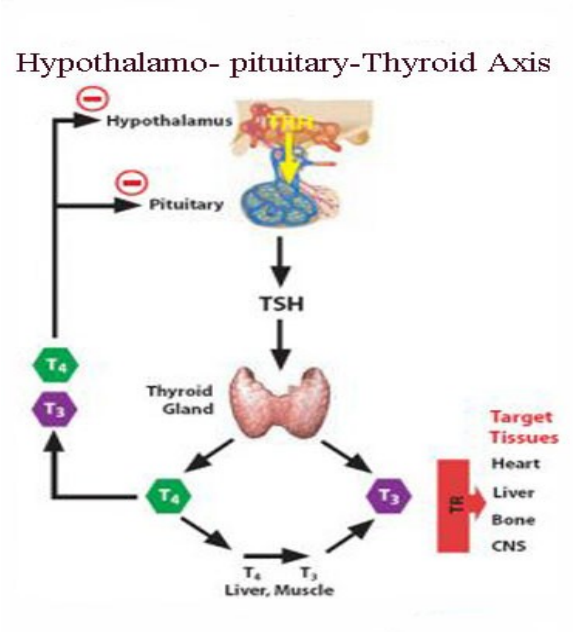
Regulation OF THYROID HORMONES

1. The hypothalamus neurosecretory cells secrete into the first capillary set of the hypothalamo-hypophyseal portal circulation the **Thyrotopin Releasing Hormone: TRH:** which is then carried by blood to the anterior pituitary cells: the thyrotropes.

TRH binds to TRH receptors of the thyrotropes producing activation of the membrane bound G proteins that activate the phospholipase enzyme.

The resulting Ca2+ & diacyl glycerol, produce finally TSH release from the thyrotropes, into the second capillary set of the hypothalamo - hypophysealportal vessels.

2. **TSH: thyroid stimulating hormone: thyrotropin:** binds to TSH serpentine receptors on the basal membrane of the thyroid gland cells leading to activation of the membrane bound G proteins, the activation of adenyl cyclase enzyme, increasing cAMP, which in turn activates the protein kinase, producing multiple phosphorylations in the thyroid cells.



Activation of the thyroid cells produce: -

A - Within 30 min: Increased proteolysis of thyroglobulin, increasing T3 &T4 in blood.

B - within hours, days, and weeks:

• Activation of iodide pump which makes intracellular to extracellular iodide about 8: 1.

Increased iodination of tyrosine & formation of thyroid hormones.

• Increased size, secretory activity and number of thyroid cells.

3. **Feedback effect of thyroid hormones.** The increased thyroid hormones produce:

A direct effect of T3 &T4 on the pituitary causing decreased production of TSH secretion. T4 that reaches the anterior pituitary is converted to T3 to exert its feed back effect.

Secondary weak effect on the hypothalamus causing a decrease in TRH secretion.